

# TRANSMITTAL FORM

Application Number 10/531,324  
Filing Date 12/20/2005  
First Named Inventor Alexandros Makriyannis  
Title Antiprotozoal Ring-Substituted Phospholipids  
Group Art Unit 1624  
Examiner Name Balasubramanian, Venkataraman  
Attorney Docket Number MAK/102/PC/US

## ENCLOSURES

- ☒ Response to Restriction Requirement ☐ Preliminary Amendment  
☐ Information Disclosure Statement ☒ Postcard reflecting enclosures  
☐ A filing fee for extra claims is calculated below:

No. of Claims Remaining After Amendment	Highest No. of Claims Previously Paid For	No. of Extra Claims	Fee For Small Entity Rate	Fee	Fee For Large Entity Rate	Fee
Total			X \$25 =		X \$50 =	
Indep.			X \$105 =		X \$210 =	
<input type="checkbox"/> First Presentation of Multiple Dependent Claims			+ \$185 =		+ \$370 =	
			TOTAL =		TOTAL =	\$

☒ It is hereby petitioned that any required extension of time be granted for filing the amendment. An extension of 5 month(s) having a fee of \$ 1,175.00 appears required.

☒ A check in the amount of \$ 1,175.00 is attached. Please credit any overpayment to Deposit Account 16-2563 of Alix, Yale & Ristas, LLP.

The Commissioner is hereby requested and authorized to charge Deposit Account 16-2563 of Alix, Yale & Ristas, LLP for any fee, not enclosed herewith, due for any reason in connection with the amendment or this or any other document accompanying the amendment, including (a) any filing fees under 37 CFR 1.16 for the presentation of extra claims and (b) any patent application processing fees under 37 CFR 1.17. A duplicate copy of this sheet is attached.

## SIGNATURE OF APPLICANT, ATTORNEY OR AGENT

Firm or Individual name Alexander E. Andrews Reg. No. 62,205  
Signature [Signature]  
Date February 20, 2009 Attorney's Docket No. MAK/102/PC/US

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I hereby certify that this correspondence is being deposited on the date below with the United States Postal Service as first class mail in an envelope addressed to "Mail Stop Amendment, Commissioner for Patents, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, Virginia 22313-1450."

Typed or Printed Name Alexander E. Andrews Reg. No. 62,205  
Signature [Signature] Date: February 20, 2009



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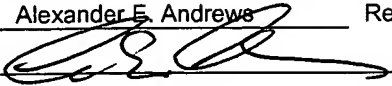
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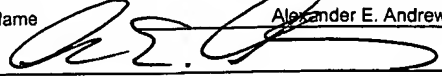
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application No. : 10/531,324  
Applicant : Alexandros Makriyannis et al.  
Filing Date : December 20, 2005  
Title : Antiprotozoal Ring-Substituted Phospholipids  
TC/A.U. : 1624  
Examiner : Balasubramanian, Venkataraman  
Docket No. : MAK/102/PC/US  
Customer No. : 002543

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Sir:

***RESPONSE TO RESTRICTION REQUIREMENT***

The Office Communication dated August 21, 2008, imposed a two-way restriction requirement between the asserted inventions of Groups:

- I. claims 1-22, drawn to compounds wherein Y is a carbocyclic ring or aromatic system, compositions and methods of use;
- II. claims 1-10, 13, 14, 21 and 22, drawn to compounds wherein Y is a heterocyclic or heteroaromatic system, compositions and methods of use.

In order to strictly comply with the Examiner's requirement in the above restriction requirement, and without agreeing to the propriety of the restriction requirement, Applicant elects the invention of Group I, including claims 1-22 drawn to compounds, compositions and methods of use.

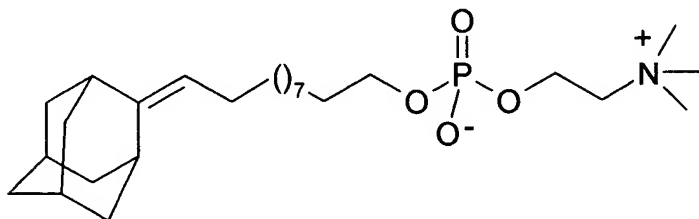
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- **The elected species**

Applicant selects the following single species within elected Group I:



- **The family proposed for examination in this application**

Applicant proposes the following family within the elected group for examination.

A compound represented by the Formula below, including isomers and stereoisomers, and physiologically acceptable salts, comprising:



wherein,

A comprises a radical selected from one of the formulae Y, YR<sup>1</sup>, R<sup>1</sup>Y, R<sup>1</sup>YR<sup>4</sup>, R<sup>1</sup>OY, YOR<sup>1</sup>, R<sup>1</sup>YOR<sup>2</sup> or R<sup>1</sup>OYOR<sup>2</sup>;

W comprises a radical of the formulae R<sup>3</sup>Q or a C4 to C7 non-aromatic heterocycle containing a nitrogen heteroatom wherein said heterocycle comprises at least one heteroatom independently selected from nitrogen, oxygen, sulfur and combinations thereof, and wherein said heterocycle can be substituted with one or more substituent groups;

Y comprises a carbocyclic ring, a carbocyclic ring comprising at least one substituent group, a fused bicyclic ring system, a fused bicyclic ring system comprising at least one substituent group, a bridged bicyclic ring system, a bridged bicyclic ring system comprising at least one substituent group, a bridged tricyclic ring system, a bridged tricyclic ring system comprising at least one

substituent group, an aromatic system or an aromatic system comprising at least one substituent group;

X comprises a valency bond, a methylene group ( $-\text{CH}_2-$ ) or a heteroatom selected from nitrogen, oxygen, sulfur;

$\text{R}^1$  comprises any possible member selected from a carbocyclic ring having about 3 to about 7 ring members, a heterocyclic ring having about 4 to about 7 ring members, an aromatic ring having about 5 to about 7 ring members, a heteroaromatic ring having about 5 to about 7 ring members,; or any above group comprising a substituent group on at least one available ring atom, an about C3 to about C20 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain, an about C3 to about C20 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain comprising one or more independently chosen heteroatoms, an about C3 to about C20 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain comprising at least one independently chosen possible member selected from a carbocyclic ring having about 4 to about 7 ring members, a heterocyclic ring having about 4 to about 7 ring members, an aromatic ring having about 5 to about 7 ring members, a heteroaromatic ring having about 5 to about 7 ring members; or any above member comprising a substituent group on at least one available ring atom, or any above about C3 to about C20 hydrocarbon chain having at least one independently chosen substituent group;

$\text{R}^2$  comprises any possible member selected from a carbocyclic ring having about 3 to about 7 ring members, a heterocyclic ring having about 4 to about 7 ring members, an aromatic ring having about 5 to about 7 ring members, a heteroaromatic ring having about 5 to about 7 ring members; any above group comprising a substituent group on at least one available ring atom, an about C2 to about C5 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain, an about C2 to about C5 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain comprising one or more independently chosen heteroatoms, an about C2 to about C5 saturated or unsaturated, straight or

branched, aliphatic hydrocarbon chain comprising at least one independently chosen possible member selected from a carbocyclic ring having about 4 to about 7 ring members, a heterocyclic ring having about 4 to about 7 ring members, an aromatic ring having about 5 to about 7 ring members, a heteroaromatic ring having about 5 to about 7 ring members; or any above member comprising a substituent group on at least one available ring atom, or any above about C2 to about C5 hydrocarbon chain having at least one independently chosen substituent group;

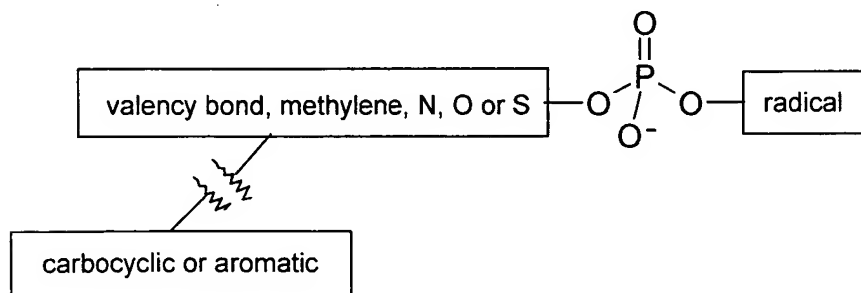
R<sup>3</sup> comprises any possible member selected from a carbocyclic ring having about 3 to about 9 ring members, a heterocyclic ring having about 4 to about 9 ring members, an aromatic ring having about 5 to about 9 ring members, a heteroaromatic ring having about 5 to about 9 ring members; any above group comprising a substituent group on at least one available ring atom, an about C2 to about C5 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain, an about C2 to about C5 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain comprising one or more independently chosen heteroatoms, an about C2 to about C5 saturated or unsaturated, straight or branched, aliphatic hydrocarbon chain comprising at least one independently chosen possible member selected from a carbocyclic ring having about 4 to about 7 ring members, a heterocyclic ring having about 4 to about 7 ring members, an aromatic ring having about 5 to about 7 ring members, a heteroaromatic ring having about 5 to about 7 ring members; or any above member comprising a substituent group on at least one available ring atom, or any above about C2 to about C5 hydrocarbon chain having at least one independently chosen substituent group;

R<sup>4</sup> comprises any group independently selected from R<sup>1</sup> or R<sup>2</sup>; and Q comprises an ammonium group, wherein said ammonium group can be substituted one or more times with a C1 to C6 alkyl radical, or comprises a C3 to C7 heterocycle containing a nitrogen heteroatom which is bonded to the R<sup>3</sup> group, wherein said heterocycle can contain one or more heteroatoms

independently selected from nitrogen, oxygen, sulfur and combinations thereof, and wherein said heterocycle can be substituted with one or more substituent groups, a heterobicyclic ring containing a nitrogen heteroatom which is bonded to the  $R^3$  group, wherein said heterobicyclic ring can contain one or more heteroatoms independently selected from nitrogen, oxygen, sulfur and combinations thereof, and wherein said heterobicyclic ring can be substituted with one or more substituent groups, a heterotricyclic ring containing a nitrogen heteroatom which is bonded to the  $R^3$  group, wherein said heterotricyclic ring can contain one or more heteroatoms independently selected from nitrogen, oxygen, sulfur and combinations thereof, and wherein said heterotricyclic ring can be substituted with one or more substituent groups. Advantageously the substituent groups are independently selected from hydroxyl, halogen, alkyl, cycloalkyl, aryl, alkoxy, alkoxycarbonyl, alkylthio or amino.

- **The family proposed for examination in this application has unity of invention**

Each of the compounds in the proposed family will share the following substantial common structure:



The Court of Appeals for the Federal Circuit, in the case of In re Watkinson, 14 USPQ2d 1407, 1409 (Fed. Cir. 1990), stated, with emphasis in original:

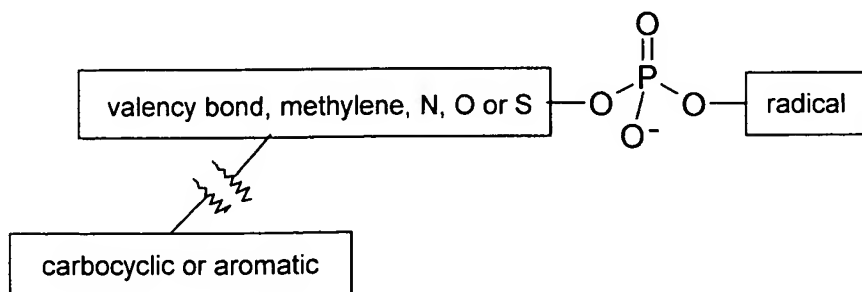
Under In re Weber, 580 F.2d 455, 458, 198 USPQ 328, 332 (CCPA 1978) and In re Haas, 580 F.2d 461, 464, 198 USPQ 334, 336 (CCPA 1978), it is *never* proper for an Examiner to reject a Markush claim under 35 U.S.C. §121. Section 121 simply does not authorize such a rejection.

The MPEP in section 803.02, acknowledging the Court decisions of In re Weber, and In re Haas states: "it is improper for the Office to refuse to examine that which Applicants regard as their invention, unless the subject matter in a claim lacks unity of invention." That section of the MPEP goes on to illustrate the examination of an elected species of a Markush claim followed by, in the proper circumstances, examination of the *non-elected species*.

Under the Court precedent of *In re Hamish* and *Ex parte Hozumi* cited by MPEP section 803.02, with bracketed text added, "unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.

The compounds within the Markush group of Applicant's proposed family (1) share a common utility: the compounds are believed to have biological activity that helps ameliorate protozoal diseases.

The compounds within the Markush group of Applicant's proposed family (2) share a substantial structural feature disclosed as being essential to that utility: the compounds share the following core structure:





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Applicant's proposed family for examination recites similar moieties for the substituent positions. For example, W recites a small family of radicals of a substantially limited number of formulae. Y has been substantially limited to various carbocyclic or aromatic ring systems. X is limited to a valency bond, methylene group or a N, O or S heteroatom. Thus, Applicant's proposed family has unity of invention and is a proper subject for examination in this application.

Further, Applicant's proposed family provides a rational, clear and concise basis from which to file and prosecute the present application as well as subsequent divisional applications.

Applicant will amend the claims to reflect the examined family once that family has been established on the record.

Pursuant to 37 CFR 1.17(a), Applicant encloses a check for \$1,175.00 for a five month extension of time.

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The Examiner is invited to telephone Applicant's attorney at 860-527-9211 if he believes further discussion is warranted and/or such discussion will hasten prosecution.

Respectfully submitted,

ALEXANDROS MAKRIYANNIS et al.

By: 

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Registration No. 62,205  
Alix, Yale & Ristas, LLP  
Attorney for Applicant

Date: February 20, 2009  
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